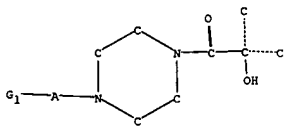
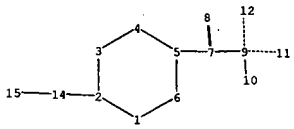
C:\Program Files\Stnexp\Queries\10069995.str





chain nodes :
7 8 10 14 15
ring nodes :
1 2 3 4 5 6
ring/chain nodes :
9 11 12
chain bonds :
2-14 5-7 7-8 7-9 9-10 9-11 9-12 14-15
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6
exact/norm bonds :
1-2 1-6 2-3 2-14 3-4 4-5 5-6 5-7 7-8 9-10 9-11 9-12 14-15
exact bonds :
7-9
isolated ring systems :
containing 1 :

G1:Cy,Ak

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS
11:CLASS 12:CLASS 14:CLASS 15:CLASS

10/069995

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=> s l1
SAMPLE SEARCH INITIATED 13:07:35 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -     26 TO ITERATE

100.0% PROCESSED      26 ITERATIONS                                2 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:          215 TO      825
PROJECTED ANSWERS:               2 TO      124

L2             2 SEA SSS SAM L1

=> s l1 sss full
FULL SEARCH INITIATED 13:07:49 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -    668 TO ITERATE

100.0% PROCESSED     668 ITERATIONS                              53 ANSWERS
SEARCH TIME: 00.00.01

L3            53 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                   148.55     148.97

FILE 'CAPLUS' ENTERED AT 13:07:56 ON 05 AUG 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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FILE COVERS 1907 - 5 Aug 2003  VOL 139 ISS 6
FILE LAST UPDATED: 4 Aug 2003  (20030804/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.


=> s l3
L4             8 L3

=> d l4 1-8 bib abs hitstr
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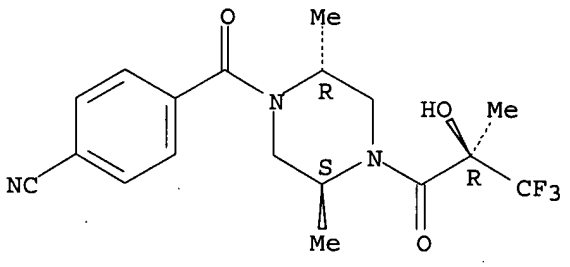
L4 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:773695 CAPLUS
DN 137:290934
TI Crystal structure of a human pyruvate dehydrogenase kinase 2 (PDHK-2) and PDHK-2 complexes with ligands and use in methods for identifying and designing new ligands
IN Knoechel, Thorsten Reginald; Robinson, Colin Mark; Taylor, Wendy Elaine; Tucker, Alexander Dunbar
PA Pfizer Limited, UK; Pfizer Inc.
SO Eur. Pat. Appl., 304 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 1247860	A1	20021009	EP 2002-252180	20020326
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2003024084	A2	20030128	JP 2002-104923	20020408
PRAI	GB 2001-8736	A	20010406		
	GB 2001-8867	A	20010409		

AB The present invention relates to crystals of human pyruvate dehydrogenase kinase 2 (PDHK-2) and to fusion proteins comprising PDHK-2. The invention also relates to high resoln. three dimensional structures of PDHK-2 in the presence or absence of physiol. and synthetic ligands obtained by x-ray diffraction and use of the structures to identify, design or select compds. that bind to PDHK-2. The invention further relates to compds. identified, designed or selected using high resoln. structures of PDHK-2. Also provided are nucleotide sequences used to obtain crystallizable PDHK-2 proteins.

IT **243982-58-3DP**, complexes with PDHK-2
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation); USES (Uses)
(crystal structure of human pyruvate dehydrogenase kinase 2 (PDHK-2) and PDHK-2 complexes with ligands and use in methods for identifying and designing new ligands)
RN 243982-58-3 CAPLUS
CN Piperazine, 1-(4-cyanobenzoyl)-2,5-dimethyl-4-[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]-, (2R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

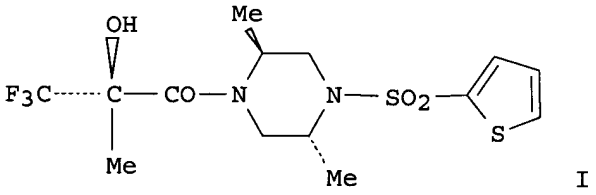


RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:185706 CAPLUS
DN 134:237497
TI N-Acyl heterocycles as inhibitors of pyruvate dehydrogenase
IN Butlin, Roger John; Pease, Janet Elizabeth; Block, Michael Howard; Nowak, Thorsten; Burrows, Jeremy Nicholas; Clarke, David Stephen
PA Astrazeneca AB, Swed.; Astrazeneca UK Ltd.
SO PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001017942	A1	20010315	WO 2000-GB3297	20000830
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1214287	A1	20020619	EP 2000-954797	20000830
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003508509	T2	20030304	JP 2001-521689	20000830
PRAI GB 1999-20821	A	19990904		
GB 1999-29835	A	19991218		
WO 2000-GB3297	W	20000830		

OS MARPAT 134:237497
GI



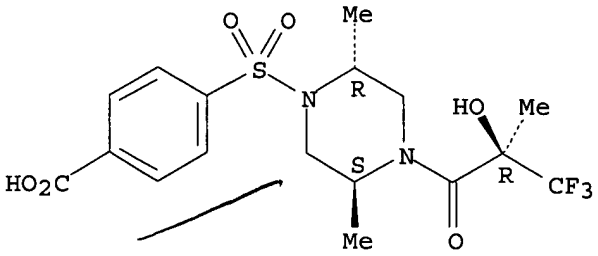
I

AB Title compds. such as (2S,2'R,5R)-I were prepd. as inhibitors of pyruvate dehydrogenase. Thus, 150 mg (R)-[(2S,5R)-2,5-dimethyl-1-(3,3,3-trifluoro-2-hydroxy-2-methylpropionyl)piperazine] was stirred with 129 mg 2-thiophenesulfonyl chloride and 0.125 mL Et3N in 25 mL EtOAc 4 h at ambient temp. to give 71 mg (2S,2'R,5R)-I. Pharmaceutical formulations were given.

IT **329794-54-9P 329794-56-1P 329794-76-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(N-acyl heterocycles as inhibitors of pyruvate dehydrogenase)

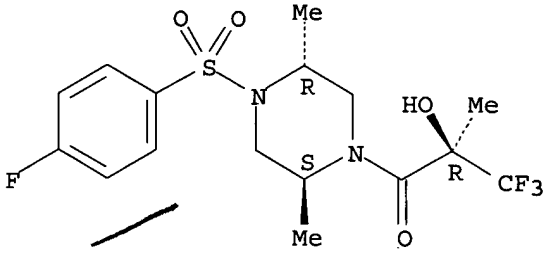
RN 329794-54-9 CAPLUS
CN Benzoic acid, 4-[[(2R,5S)-2,5-dimethyl-4-[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]-1-piperazinyl]sulfonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



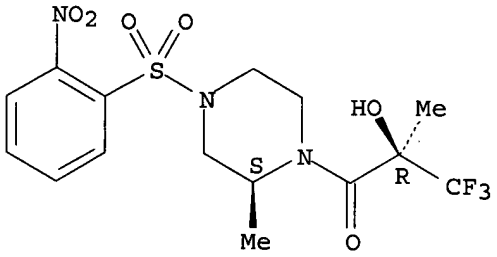
RN 329794-56-1 CAPLUS
CN Piperazine, 1-[(4-fluorophenyl)sulfonyl]-2,5-dimethyl-4-[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]-, (2R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



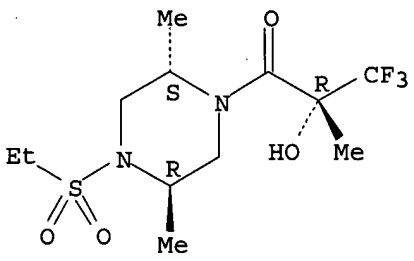
RN 329794-76-5 CAPLUS
CN Piperazine, 2-methyl-4-[(2-nitrophenyl)sulfonyl]-1-[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



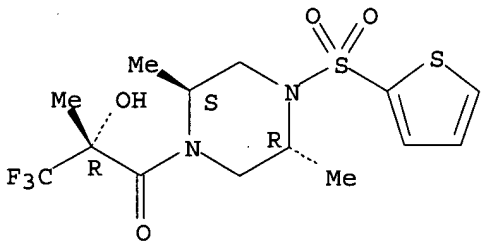
IT **329794-52-7P 329794-53-8P 329794-55-0P**
329794-57-2P 329794-60-7P 329794-61-8P
329794-62-9P 329794-63-0P 329794-64-1P
329794-65-2P 329794-66-3P 329794-67-4P
329794-68-5P 329794-69-6P 329794-72-1P
329794-73-2P 329794-74-3P 329794-75-4P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(N-acyl heterocycles as inhibitors of pyruvate dehydrogenase)
RN 329794-52-7 CAPLUS
CN Piperazine, 1-(ethylsulfonyl)-2,5-dimethyl-4-[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]-, (2R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



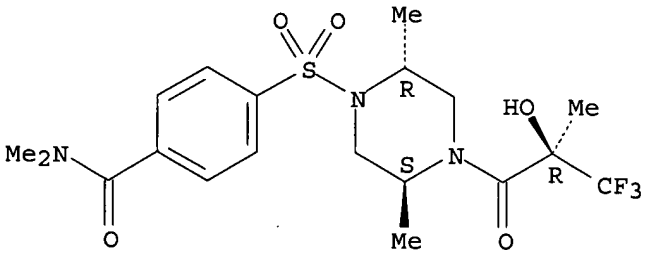
RN 329794-53-8 CAPLUS
CN Piperazine, 2,5-dimethyl-1-(2-thienylsulfonyl)-4-[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]-, (2R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



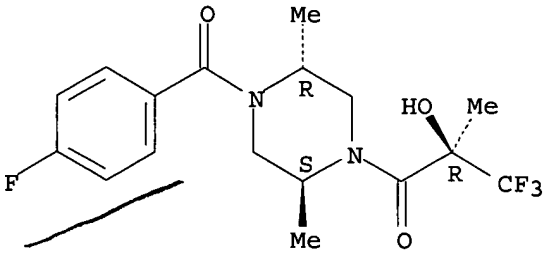
RN 329794-55-0 CAPLUS
CN Benzamide, 4-[[(2R,5S)-2,5-dimethyl-4-[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]-1-piperazinyl]sulfonyl]-N,N-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



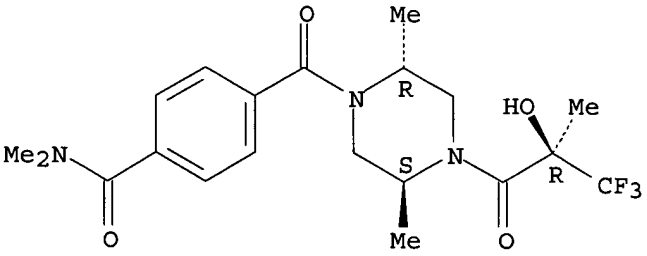
RN 329794-57-2 CAPLUS
CN Piperazine, 1-(4-fluorobenzoyl)-2,5-dimethyl-4-[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]-, (2R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



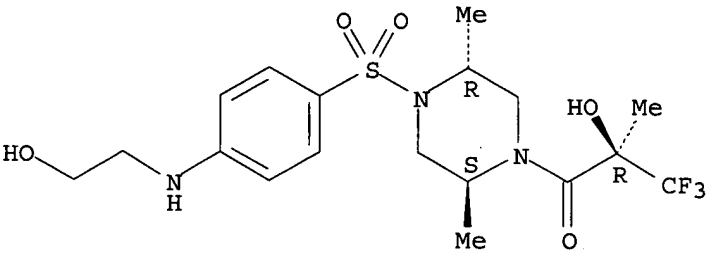
RN 329794-60-7 CAPLUS
CN Benzamide, 4-[[(2R,5S)-2,5-dimethyl-4-[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]-1-piperazinyl]carbonyl]-N,N-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



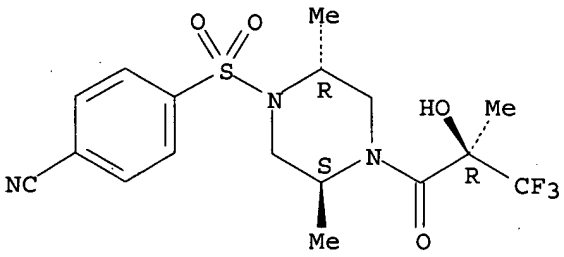
RN 329794-61-8 CAPLUS
CN Piperazine, 1-[[4-[(2-hydroxyethyl)amino]phenyl]sulfonyl]-2,5-dimethyl-4-[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]-, (2R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



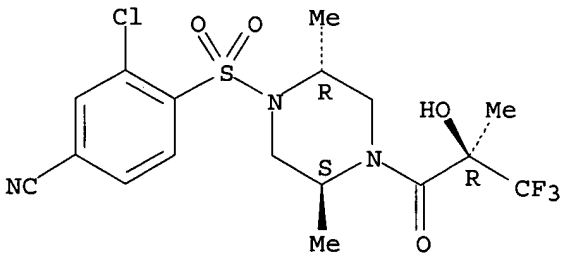
RN 329794-62-9 CAPLUS
CN Piperazine, 1-[(4-cyanophenyl)sulfonyl]-2,5-dimethyl-4-[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]-, (2R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



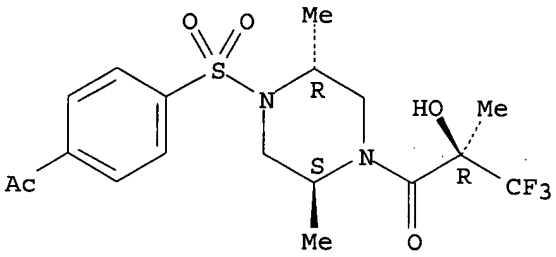
RN 329794-63-0 CAPLUS
CN Piperazine, 1-[(2-chloro-4-cyanophenyl)sulfonyl]-2,5-dimethyl-4-[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]-, (2R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



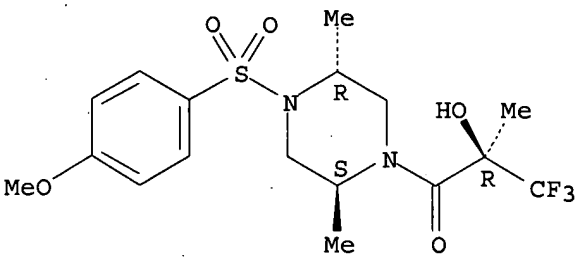
RN 329794-64-1 CAPLUS
CN Piperazine, 1-[(4-acetylphenyl)sulfonyl]-2,5-dimethyl-4-[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]-, (2R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



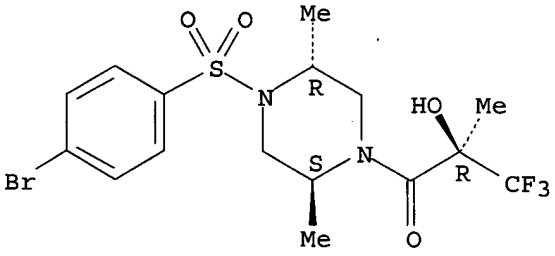
RN 329794-65-2 CAPLUS
CN Piperazine, 1-[(4-methoxyphenyl)sulfonyl]-2,5-dimethyl-4-[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]-, (2R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



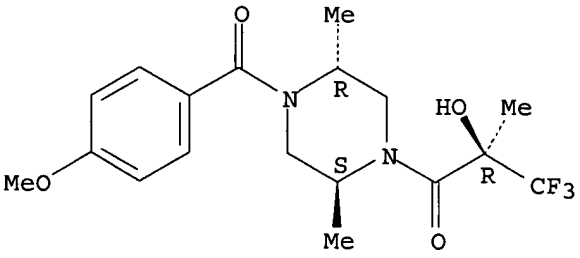
RN 329794-66-3 CAPLUS
CN Piperazine, 1-[(4-bromophenyl)sulfonyl]-2,5-dimethyl-4-[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]-, (2R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



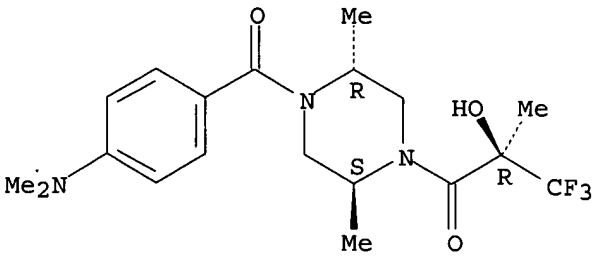
RN 329794-67-4 CAPLUS
CN Piperazine, 1-(4-methoxybenzoyl)-2,5-dimethyl-4-[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]-, (2R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



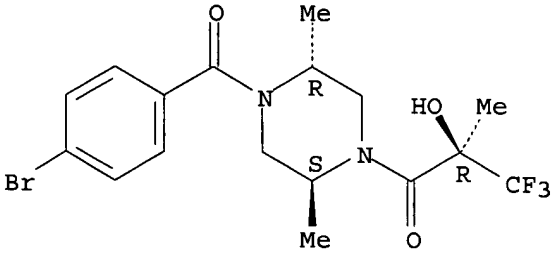
RN 329794-68-5 CAPLUS
CN Piperazine, 1-[4-(dimethylamino)benzoyl]-2,5-dimethyl-4-[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]-, (2R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



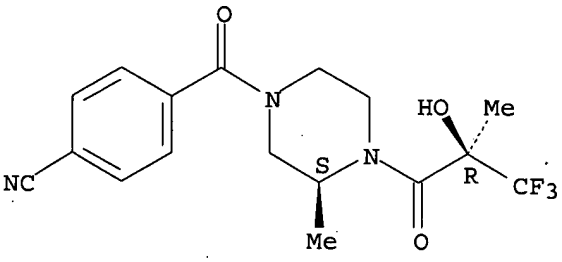
RN 329794-69-6 CAPLUS
CN Piperazine, 1-(4-bromobenzoyl)-2,5-dimethyl-4-[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]-, (2R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



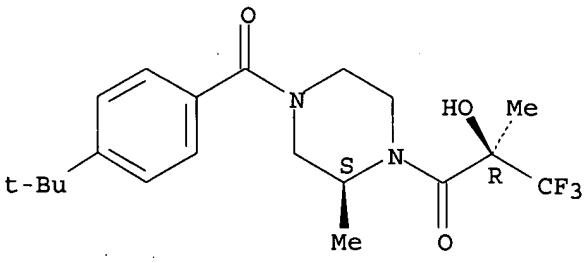
RN 329794-72-1 CAPLUS
CN Piperazine, 4-(4-cyanobenzoyl)-2-methyl-1-[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



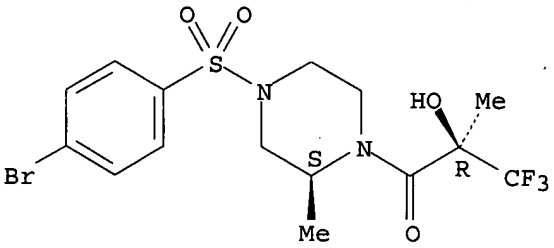
RN 329794-73-2 CAPLUS
CN Piperazine, 4-[4-(1,1-dimethylethyl)benzoyl]-2-methyl-1-[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



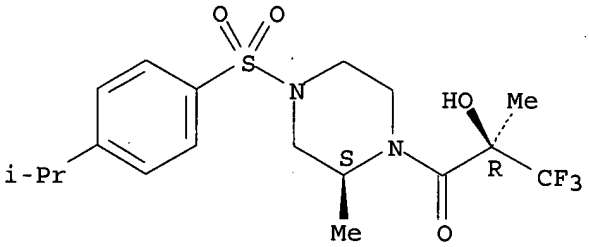
RN 329794-74-3 CAPLUS
CN Piperazine, 4-[(4-bromophenyl)sulfonyl]-2-methyl-1-[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 329794-75-4 CAPLUS
CN Piperazine, 2-methyl-4-[[4-(1-methylethyl)phenyl]sulfonyl]-1-[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]-, (2S)- (9CI) (CA INDEX NAME)

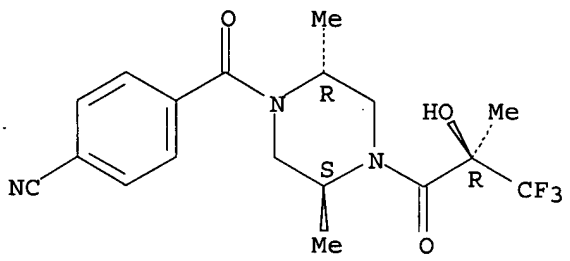
Absolute stereochemistry.



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:469974 CAPLUS
DN 133:277917
TI Diverse mechanisms of inhibition of pyruvate dehydrogenase kinase by structurally distinct inhibitors
AU Mann, W. R.; Dragland, C. J.; Vinluan, C. C.; Vedananda, T. R.; Bell, P. A.; Aicher, T. D.
CS Metabolic and Cardiovascular Diseases Research, Novartis Institute for Biomedical Research, Summit, NJ, 07901-1398, USA
SO Biochimica et Biophysica Acta (2000), 1480(1-2), 283-292
CODEN: BBACAQ; ISSN: 0006-3002
PB Elsevier Science B.V.
DT Journal
LA English
AB The mechanism of action of structurally distinct pyruvate dehydrogenase kinase (PDK) inhibitors was examd. in assays with exptl. contexts ranging from an intact pyruvate dehydrogenase complex (PDC) with and without supplemental ATP or ADP to a synthetic peptide substrate to PDK autophosphorylation. Some compds. directly inhibited the catalytic activity of PDKs. Some of the inhibitor classes tested inhibited autophosphorylation of recombinant PDK1 and PDK2. During these studies, PDC was shown to be directly inhibited by a novel mechanism; the addn. of supplemental recombinant PDKs, an effect that is ADP-dependent and partly alleviated by members of each of the compd. classes tested. Overall, these data demonstrate that small mols. acting at diverse sites can inhibit PDK activity.
IT **243982-58-3**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(diverse mechanisms of inhibition of pyruvate dehydrogenase kinase by structurally distinct inhibitors)
RN 243982-58-3 CAPLUS
CN Piperazine, 1-(4-cyanobenzoyl)-2,5-dimethyl-4-[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]-, (2R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

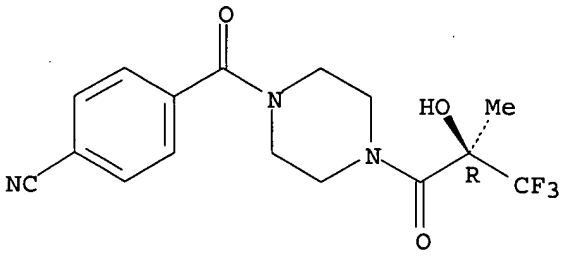


prov. out

RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

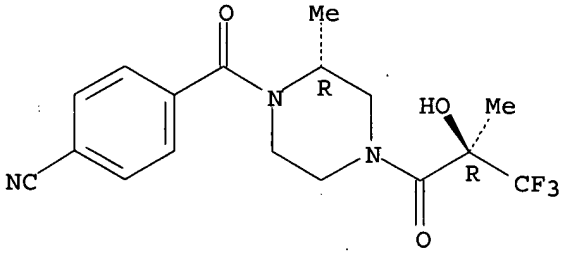
L4 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:60177 CAPLUS
DN 132:189302
TI Secondary Amides of (R)-3,3,3-Trifluoro-2-hydroxy-2-methylpropionic Acid as Inhibitors of Pyruvate Dehydrogenase Kinase
AU Aicher, Thomas D.; Anderson, Robert C.; Gao, Jiaping; Shetty, Suraj S.; Coppola, Gary M.; Stanton, James L.; Knorr, Douglas C.; Sperbeck, Donald M.; Brand, Leonard J.; Vinluan, Christine C.; Kaplan, Emma L.; Dragland, Carol J.; Tomaselli, Hollis C.; Islam, Amin; Lozito, Robert J.; Liu, Xilin; Maniara, Wieslawa M.; Fillers, William S.; DelGrande, Dominick; Walter, R. Eric; Mann, William R.
CS Novartis Institute for Biomedical Research, Summit, NJ, 07901, USA
SO Journal of Medicinal Chemistry (2000), 43(2), 236-249
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
OS CASREACT 132:189302
AB N'-Methyl-N-(4-tert-butyl-1,2,5,6-tetrahydropyridine)thiourea, SDZ048-619, is a modest inhibitor (IC50 = 180 .mu.M) of pyruvate dehydrogenase kinase (PDHK). In an optimization of the N-methylcarbothioamide moiety of SDZ048-619, it was discovered that amides with a small acyl group, in particular appropriately substituted amides of (R)-3,3,3-trifluoro-2-hydroxy-2-methylpropionic acid, are inhibitors of PDHK. Utilizing this acyl moiety, herein is reported the rationale leading to the optimization of a series of acylated piperazine derivs. Me substitution of the piperazine at the 2- and 5-positions (with S and R abs. stereochem.) markedly increased the potency of the lead compd. (>1000-fold). Oral bioavailability of the compds. in this series is good and is optimal (as measured by AUC) when the 4-position of the piperazine is substituted with an electron-poor benzoyl moiety. (+)-1-N-[2,5-(S,R)-Dimethyl-4-N-(4-cyanobenzoyl)piperazine]-(R)-3,3,3-trifluoro-2-hydroxy-2-methylpropanamide inhibits PDHK in the primary enzymic assay with an IC50 of 16 nM, enhances the oxidn. of [14C]lactate into 14CO2 in human fibroblasts with an EC50 of 57 nM, diminishes lactate significantly 2.5 h post-oral-dose at doses as low as 1 .mu.mol/kg, and increases the ex vivo activity of pyruvate dehydrogenase in muscle, liver, and fat tissues in normal Sprague-Dawley rats. These PDHK inhibitors, however, do not lower glucose in diabetic animal models.
IT **243982-52-7P 243982-55-0P 243982-56-1P**
243982-58-3P 260254-22-6P 260254-23-7P
260254-24-8P 260254-27-1P 260254-30-6P
260254-31-7P 260254-32-8P 260254-34-0P
260254-35-1P 260254-37-3P 260254-38-4P
260254-39-5P 260254-40-8P 260254-41-9P
260254-42-0P 260254-49-7P 260254-51-1P
260254-53-3P 260254-54-4P 260254-56-6P
260254-57-7P 260254-58-8P 260254-59-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(secondary amides of (R)trifluorohydroxymethylpropionic acid as inhibitors of pyruvate dehydrogenase kinase in relation to structure and treatment of diabetes)
RN 243982-52-7 CAPLUS
CN Piperazine, 1-(4-cyanobenzoyl)-4-[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



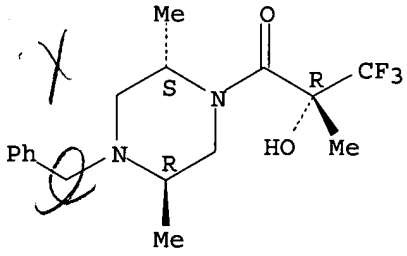
RN 243982-55-0 CAPLUS
CN Piperazine, 1-(4-cyanobenzoyl)-2-methyl-4-[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



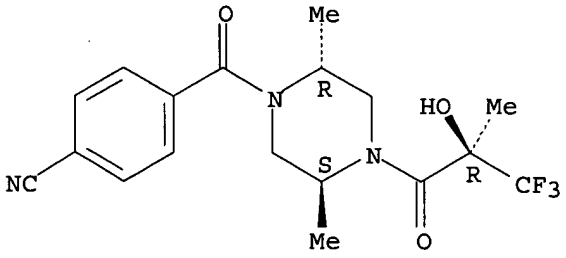
RN 243982-56-1 CAPLUS
CN Piperazine, 2,5-dimethyl-1-(phenylmethyl)-4-[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]-, (2R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



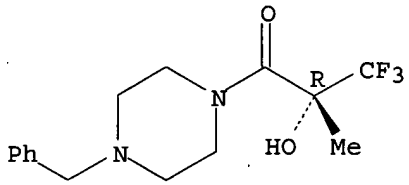
RN 243982-58-3 CAPLUS
CN Piperazine, 1-(4-cyanobenzoyl)-2,5-dimethyl-4-[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]-, (2R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

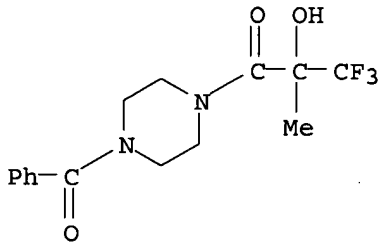


RN 260254-22-6 CAPLUS
CN Piperazine, 1-(phenylmethyl)-4-[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]- (9CI) (CA INDEX NAME)

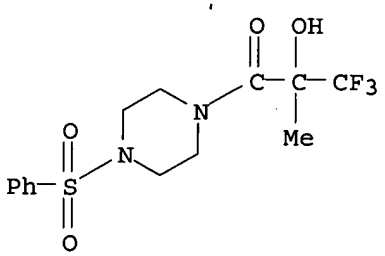
Absolute stereochemistry.



RN 260254-23-7 CAPLUS
CN Piperazine, 1-benzoyl-4-(3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl)- (9CI) (CA INDEX NAME)

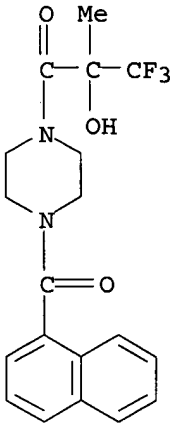


RN 260254-24-8 CAPLUS
CN Piperazine, 1-(phenylsulfonyl)-4-(3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl)- (9CI) (CA INDEX NAME)



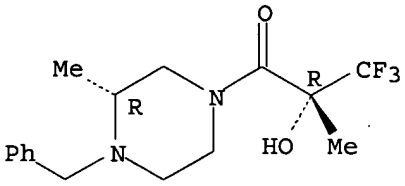
RN 260254-27-1 CAPLUS

CN Piperazine, 1-(1-naphthalenylcarbonyl)-4-(3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl)- (9CI) (CA INDEX NAME)



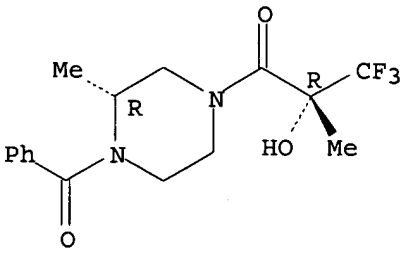
RN 260254-30-6 CAPLUS
CN Piperazine, 2-methyl-1-(phenylmethyl)-4-[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



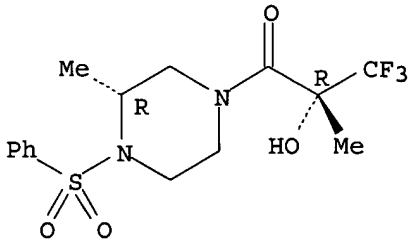
RN 260254-31-7 CAPLUS
CN Piperazine, 1-benzoyl-2-methyl-4-[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



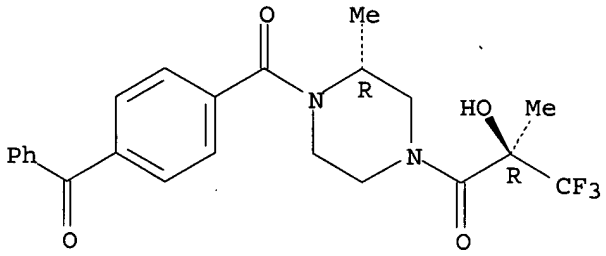
RN 260254-32-8 CAPLUS
CN Piperazine, 2-methyl-1-(phenylsulfonyl)-4-[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



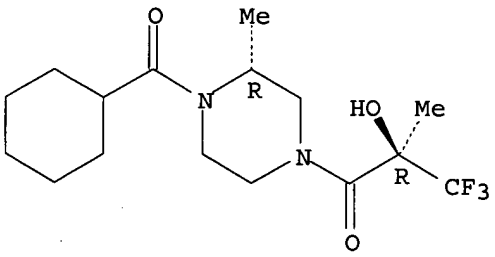
RN 260254-34-0 CAPLUS
CN Piperazine, 1-(4-benzoylbenzoyl)-2-methyl-4-[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



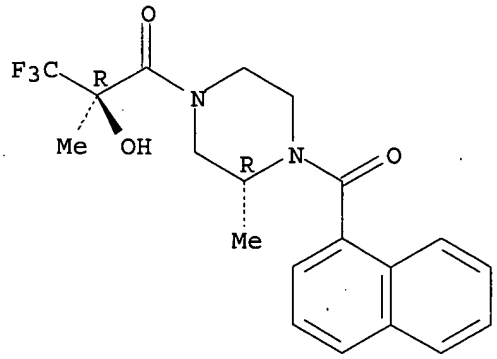
RN 260254-35-1 CAPLUS
CN Piperazine, 1-(cyclohexylcarbonyl)-2-methyl-4-[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



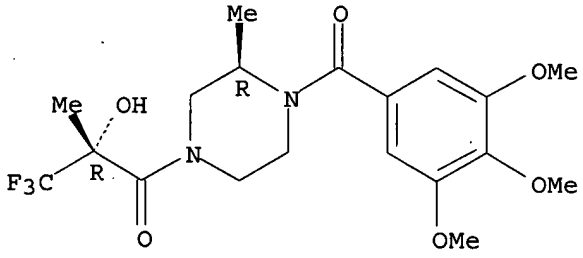
RN 260254-37-3 CAPLUS
CN Piperazine, 2-methyl-1-(1-naphthalenylcarbonyl)-4-[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



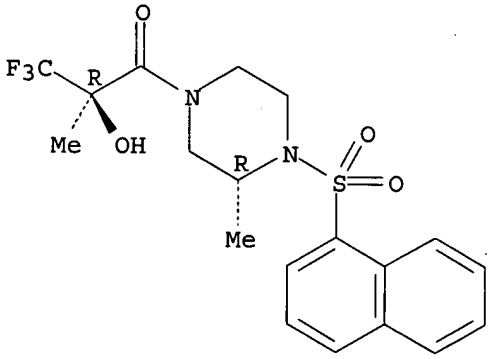
RN 260254-38-4 CAPLUS
CN Piperazine, 2-methyl-4-[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]-1-(3,4,5-trimethoxybenzoyl)-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



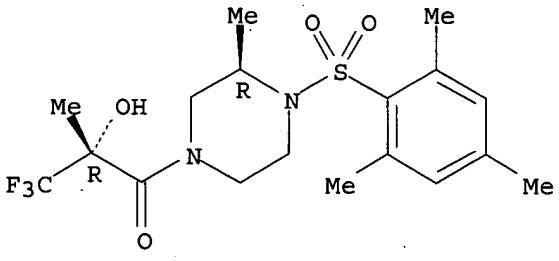
RN 260254-39-5 CAPLUS
CN Piperazine, 2-methyl-1-(1-naphthalenylsulfonyl)-4-[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



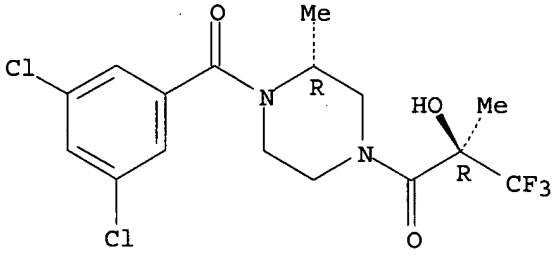
RN 260254-40-8 CAPLUS
CN Piperazine, 2-methyl-4-[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]-1-[(2,4,6-trimethylphenyl)sulfonyl]-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



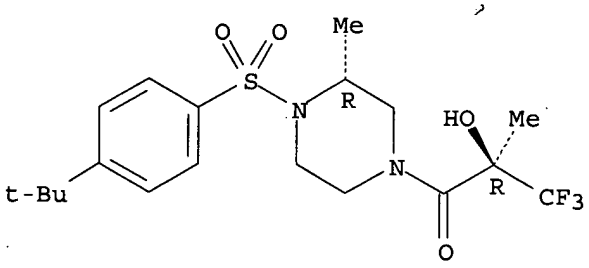
RN 260254-41-9 CAPLUS
CN Piperazine, 1-(3,5-dichlorobenzoyl)-2-methyl-4-[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



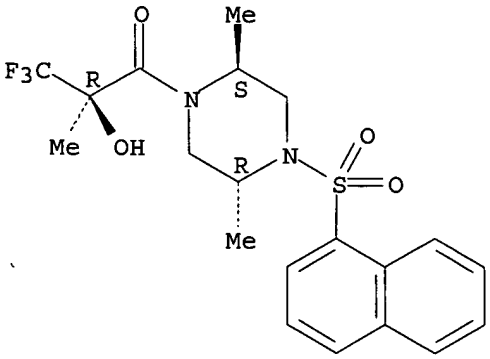
RN 260254-42-0 CAPLUS
CN Piperazine, 1-[[4-(1,1-dimethylethyl)phenyl]sulfonyl]-2-methyl-4-[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



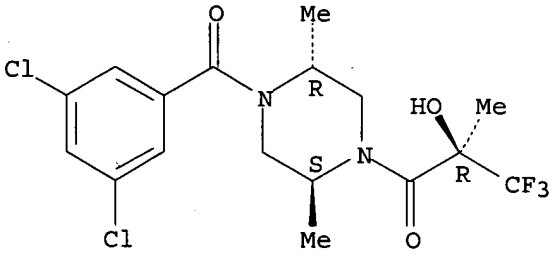
RN 260254-49-7 CAPLUS
CN Piperazine, 2,5-dimethyl-1-(1-naphthalenylsulfonyl)-4-[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]-, (2R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



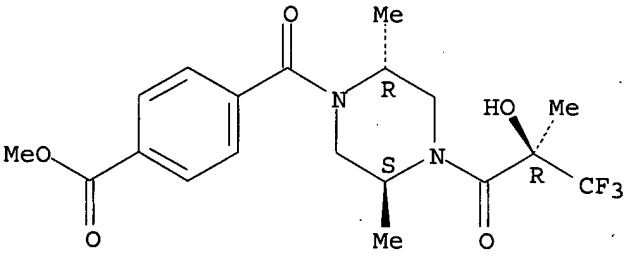
RN 260254-51-1 CAPLUS
CN Piperazine, 1-(3,5-dichlorobenzoyl)-2,5-dimethyl-4-[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]-, (2R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



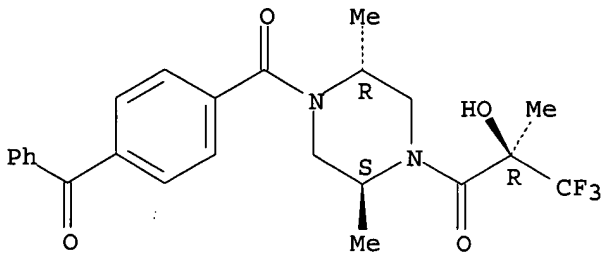
RN 260254-53-3 CAPLUS
CN Benzoic acid, 4-[[(2R,5S)-2,5-dimethyl-4-[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]-1-piperazinyl]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



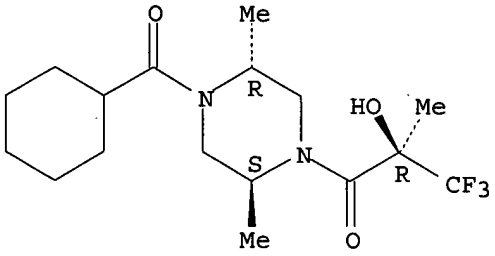
RN 260254-54-4 CAPLUS
CN Piperazine, 1-(4-benzoylbenzoyl)-2,5-dimethyl-4-[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]-, (2R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



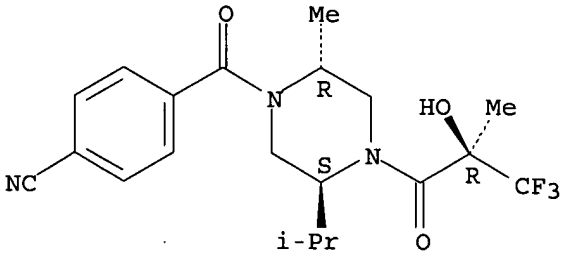
RN 260254-56-6 CAPLUS
CN Piperazine, 1-(cyclohexylcarbonyl)-2,5-dimethyl-4-[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]-, (2R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



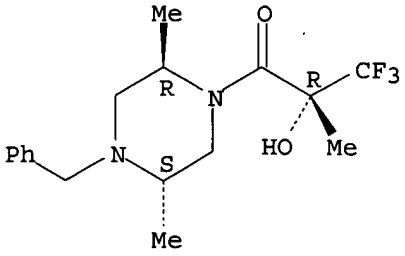
RN 260254-57-7 CAPLUS
CN Piperazine, 1-(4-cyanobenzoyl)-2-methyl-5-(1-methylethyl)-4-[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]-, (2R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



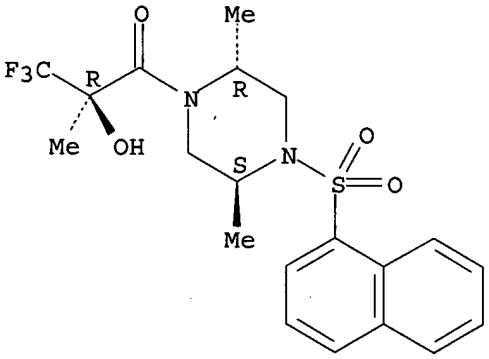
RN 260254-58-8 CAPLUS
CN Piperazine, 2,5-dimethyl-1-(phenylmethyl)-4-[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



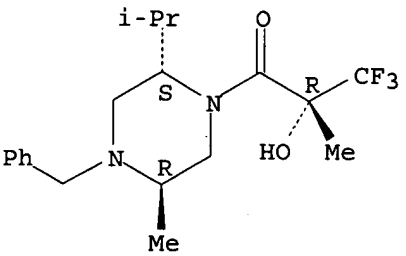
RN 260254-59-9 CAPLUS
CN Piperazine, 2,5-dimethyl-1-(1-naphthalenylsulfonyl)-4-[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **260254-76-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(secondary amides of (R)trifluorohydroxymethylpropionic acid as inhibitors of pyruvate dehydrogenase kinase in relation to structure and treatment of diabetes)
RN 260254-76-0 CAPLUS
CN Piperazine, 2-methyl-5-(1-methylethyl)-1-(phenylmethyl)-4-[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]-, (2R,5S)- (9CI) (CA INDEX NAME)

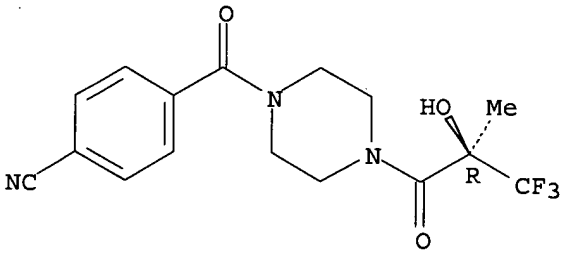
Absolute stereochemistry.



RE.CNT 75 THERE ARE 75 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

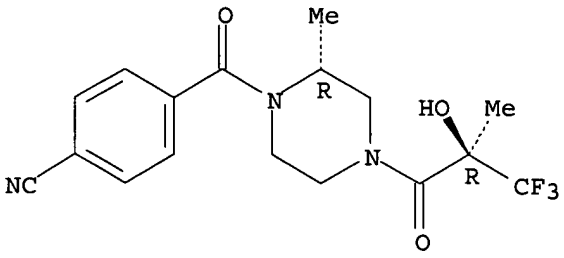
L4 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:436784 CAPLUS
DN 131:222995
TI (R)-3,3,3-Trifluoro-2-hydroxy-2-methylpropionamides Are Orally Active Inhibitors of Pyruvate Dehydrogenase Kinase
AU Aicher, Thomas D.; Anderson, Robert C.; Bebernitz, Gregory R.; Coppola, Gary M.; Jewell, Charles F.; Knorr, Douglas C.; Liu, Charles; Sperbeck, Donald M.; Brand, Leonard J.; Strohschein, Robert J.; Gao, Jiaping; Vinluan, Christine C.; Shetty, Suraj S.; Dragland, Carol; Kaplan, Emma L.; DelGrande, Dominick; Islam, Amin; Liu, Xilin; Lozito, Robert J.; Maniara, Wieslawa M.; Walter, R. Erik; Mann, William R.
CS Novartis Institute for Biomedical Research, Summit, NJ, 07901, USA
SO Journal of Medicinal Chemistry (1999), 42(15), 2741-2746
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
AB Diverse amides of (R)-3,3,3-trifluoro-2-hydroxy-2-methylpropionic acid were inhibitors of pyruvate dehydrogenase kinase (PDHK) without halogens .alpha.,.alpha. to a carbonyl. In addn. to the probable reduced toxicity due to not having halogens .alpha. to a carbonyl, these compds. were more potent in the primary enzymic assay than any of the previously reported compds. by up to 500-fold. They are the first compds. other than dichlorinated halogenated acids known to be active in a cellular assay. Some of the amides were potent and orally bioavailable inhibitors of PDHK in vivo. The expected consequence of PDHK inhibition, the activation of the pyruvate dehydrogenase complex, was obsd. indirectly in vivo by measuring the lowering of lactate in normal 24-h fasted rats after oral dosing. These compds. will allow further pharmacol. investigation of the effect of increasing oxidative disposal of lactate and pyruvate in disease states such as diabetes, ischemia, endotoxic or hemorrhagic shock, lactic acidosis and cardiac insufficiency.
IT **243982-52-7P 243982-55-0P 243982-56-1P 243982-58-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of trifluorohydroxymethylpropionamides as orally active inhibitors of pyruvate dehydrogenase kinase)
RN 243982-52-7 CAPLUS
CN Piperazine, 1-(4-cyanobenzoyl)-4-[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



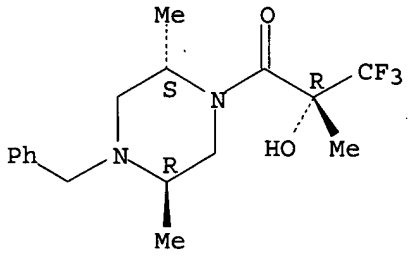
RN 243982-55-0 CAPLUS
CN Piperazine, 1-(4-cyanobenzoyl)-2-methyl-4-[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



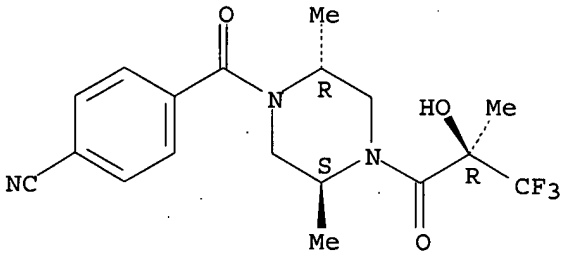
RN 243982-56-1 CAPLUS
CN Piperazine, 2,5-dimethyl-1-(phenylmethyl)-4-[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]-, (2R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 243982-58-3 CAPLUS
CN Piperazine, 1-(4-cyanobenzoyl)-2,5-dimethyl-4-[(2R)-3,3,3-trifluoro-2-hydroxy-2-methyl-1-oxopropyl]-, (2R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

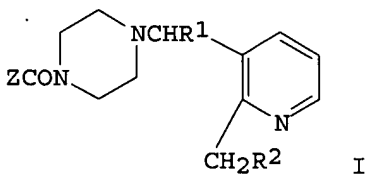


RE.CNT 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1993:539266 CAPLUS
DN 119:139266
TI (2-alkyl-3-pyridyl)methylpiperazine derivatives as platelet activating factor (PAF) antagonists
IN Carceller, Elena; Jimenez, Pere J.; Recasens, Nuria; Almansa, Carmen; Bartroli, Javier
PA Uriach, J., y Cia. S.A., Spain
SO Eur. Pat. Appl., 78 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 528172	A1	19930224	EP 1992-111986	19920714
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, PT, SE				
	ES 2036926	A1	19930601	ES 1991-1855	19910808
	ES 2036926	B1	19940116		
	JP 05213879	A2	19930824	JP 1992-229142	19920805
	CA 2075673	AA	19930209	CA 1992-2075673	19920810
PRAI	ES 1991-1855		19910808		

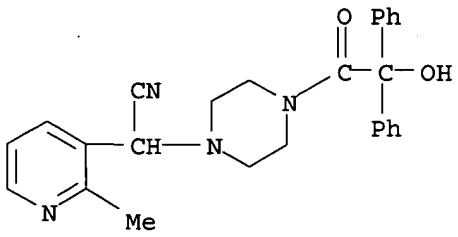
OS MARPAT 119:139266
GI



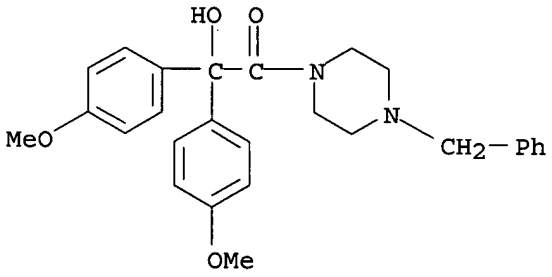
I

AB Title compds. I (R1 = cyano, R3O2C, (R3)2NCO, R3CO, R3C.tplbond.C, R3ON:CR3, wherein R3 = H, C1-6 alkyl; R2 = H, C1-3 alkyl; Z = R4R5R6C(CH2)n wherein n = 0-2; R4 = H, C1-6 alkyl, (substituted) Ph or 5-6-membered heterocyclyl, R5 = H, C1-6 alkyl, F3C, etc., R6 = H, C1-6 alkyl, (substituted) amino, etc.), and salts thereof useful as PAF antagonists, are prepd. To I (R1 = cyano, R2 = Me, Z = H2NCHPhCH2) (prepn. given) in MeOH was added PhCHO, followed by MeOH/HCl to adjust the pH to 6-7, after which was added NaBH3CN, the mixt. was stirred at room temp. for 18 h, the solvent removed and 0.1 N NaOH added to give I (R1 = cyano, R2 = Me, Z = PhCH2NHCHPhCH2) (II). In test for inhibition of platelet aggregation induced by PAF the IC50 of II was 0.0091 .mu.M. Addnl. I were prepd. and tested also for inhibition of hypotensive effect and mortality induced by PAF. Pharmaceutical formulations comprising I are given.

IT **149691-88-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as platelet activating factor antagonist)
RN 149691-88-3 CAPLUS
CN 1-Piperazineacetonitrile, 4-(hydroxydiphenylacetyl)-.alpha.-(2-methyl-3-pyridinyl)- (9CI) (CA INDEX NAME)

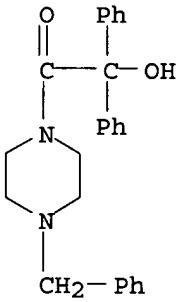

O
Ph
C
C
OH
Ph
CN
CH
N
N
N
Me

L4 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1972:46165 CAPLUS
DN 76:46165
TI Synthesis of basic amides derived from .alpha.,.alpha.-bis(4-methoxyphenyl)glycolicacid
AU Rylski, Leszek; Kozakiewicz, Irena; Gorczyca, Eugenia; Mrowicka, Maria; Rzepecka, Krystyna
CS Akad. Med., Gdansk, Pol.
SO Acta Poloniae Pharmaceutica (1971), 28(3), 267-72
CODEN: APPHAX; ISSN: 0001-6837
DT Journal
LA Polish
GI For diagram(s), see printed CA Issue.
AB I and II were prepd. for biol. testing for spasmolytic activity as structural analogs of adiphenine and hexahydroadiphenine. N-Substituted piperazine in anhyd. C6H6 treated under cooling with 1 mole ClCOCO2Et and the mixt. refluxed 2 hr yielded 37% I-HCl (R=PhCH2CH2) or 61% I-HCl (R=PhCH2). The above I (yields 93 and 90%, resp.) as well as 77% I-HCl (R=Ph) were also prepd. in a similar reaction with (CO2Et)2. Grignard reaction between p-MeOC6H4MgI and I (liberated from I-HCl with K2CO3 and extd. with Et2O) gave upon hydrolysis with 25% aq. NH4Cl 31-69% II (R=PhCH2CH2; R=PhCH2; R=Ph).
IT **35219-10-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 35219-10-4 CAPLUS
CN Piperazine, 1-[hydroxybis(4-methoxyphenyl)acetyl]-4-(phenylmethyl)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

L4 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1968:86028 CAPLUS
DN 68:86028
TI Hypocholesteremic agents. IV. Substituted piperazines
AU Wright, Howard Bernard; Martin, Donald Lyons
CS Res. Div., Abbott Lab., N. Chicago, IL, USA
SO Journal of Medicinal Chemistry (1968), 11(2), 390-1
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English
AB Compds. (24) related to chlorocyclizine and N-[.beta.-phenyl-.beta.-(3-chlorophenyl)-.beta.-hydroxyethyl)-N'-methylpiperazine were prepd. and tested for activity in reducing the blood cholesterol concn. in mice. The compds. had varying degrees of activity for the lowering of blood cholesterol, but the lowering was accompanied in general by an increased cellular mass in the liver.
IT **19178-71-3**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(hypocholesteremic activity of)
RN 19178-71-3 CAPLUS
CN Piperazine, 1-benziloyl-4-benzyl-, monohydrochloride (8CI) (CA INDEX NAME)



HCl

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FULL ESTIMATED COST                                    40.04     189.01

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  printed between 1907-1966 are available in the PAGE
  display formats.

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  all substance data from the REGISTRY file.  Enter HELP FIRST for
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L5              0 L3

=> log h
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                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.40     189.41

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                     0.00      -5.21

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